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Treatment of Endometriosis

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Author and Editor

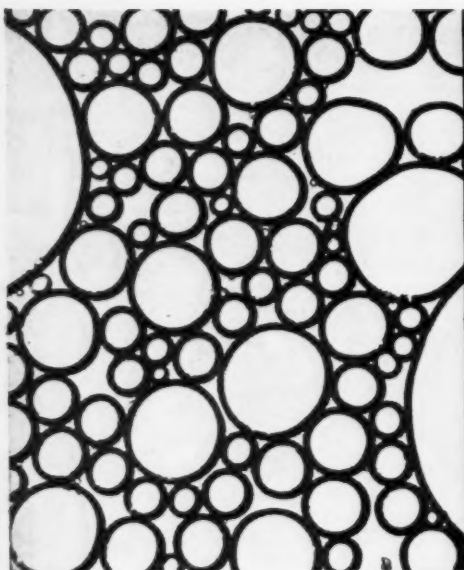
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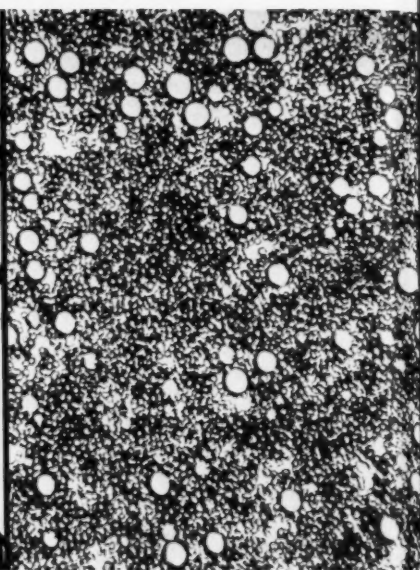
VOLUME 59, NUMBER 12

DECEMBER 1952

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59th year of publication

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2. Turell, R.: *New York St. J. M.* 50:2282, 1950.
3. Heimer, C. B., Grayzel, H. G., and Kramer, B.: *Archives Pediat.* 68:382, 1951.

Author and Editor

FREDERIC R. STEARNS, M.D., *Editor*

When one has seen a considerable number of medical manuscripts in the course of many years, he wonders about the best way to convey medical experience to readers. Authors and readers may have different viewpoints. Most authors want to cover a subject extensively. Most readers prefer a succinct and concise presentation. Most editors are caught in between.

The history of medicine has demonstrated that many investigators and clinical observers with new ideas were "burnt at the stake." In his latest book *The Story of the Adaptation Syndrome*, Hans Selye writes on page 209: "Many of you will remember the innumerable criticisms of which I became a target when I first formulated the concept of the diseases of adaptation." (*Acta, Inc. Montreal, Canada, 1952*). This is one of the latest examples. The earliest may go back to the physicians whose observations may be inscribed in the Ebers papyrus. It

has taken years or decades and even centuries to vindicate novel statements. Medicine again is in an era of great evolution. One should be quite careful in passing judgement on new, even apparently inconsistent approaches. It may even be preferable to occasionally publish a paper which may later turn out to be a misconception rather than to miss one which may be a basis of advance.

According to the purpose and program of his journal, it is, of course, the editor's task to select submitted papers in order to offer the reader a related variety of subjects in each issue. This requires also a judicious timing of articles to be published, which, unfortunately, does not always conform to the tempo with which the author wishes to see his paper published.

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It has become a habit in medical writing to stud articles with literature references. While it may be wise to discuss those previous papers

which have a pertinent connection with the present exposition, it is hardly necessary to start with Hippocrates and to burden the reader with the enumeration of all the published articles on the topic. It makes reading cumbersome, it thwarts the originality of the discourse, and it deviates the reader's attention from the author's own viewpoint. We feel, therefore, it would be wise to limit the literature references to the indispensable.

Another frequent feature of medical writing is the length of the article. Not too rarely repetitions of the same theme appear in various parts of the paper which could have been omitted by a planned composition and a self-critical styling. Repetitions do not enhance evidence, they disperse it.

It may sound heretic, but we are not in favor of "summaries". Papers, in our opinion, should be read in full. Summaries are invitations to pass over the paper and to be satisfied with a conveniently presented extract. We have often found it a criterion of a too lengthy exposition when the author succeeded in summarizing the purport of his article so that it comprised all the essential factors. It would have been preferable in the interest of the reader to restrict the entire paper to the essential rather than to abstract, at the end, the essential from the non-essential.

A big stumbling block in medical writing is often the terminology. Many diseases or syndromes have

various designations, which, however, confer no different meanings. It may be just the author's predilection for one or the other term which determines its use in the paper. Some authors are dissatisfied with the fluctuating terminology and try to solve this predicament by introducing a new term. Instead of simplifying the understanding, it only increases the confusion. Admittedly many terms, presently employed, are either obsolete, lacking in precision, or not in accord with actual scientific knowledge. As long as there is no agreement on a uniform and universal terminology, it is better to use terms that are generally understood in order not to confuse the issues.

At times, one is confronted with the question whether so many different medical publications are justified. We have taken the stand that they are. Medicine always has been considered an art, based on changing scientific foundations. As all arts, medicine is essentially individualistic. Only the experience, initiative, and intuition of each and every one of the many, at the bedside, at the clinic, in the hospital, in the laboratory, can illuminate all facets of a problem.

Many important observations, many guiding ideas, many methodological improvements would never have become the general property of the profession if there were not a great number of medical publications.

Further Report on A New Treatment for Endometriosis

*Vitaminized, micronized stilbestrol
or micronized stilbestrol are used with
success in treatment of endometriosis*

KARL JOHN KARNAKY, M.D., *Menstrual Disorder Clinic,
Research Division, Jefferson Davis Hospital and
Baylor University College of Medicine, Houston, Texas**

Diethylstilbestrol has been demonstrated to be of use in a great variety of conditions encountered in obstetrics and gynecology. In obstetrical practice it has proven to be the most valuable drug for the prevention of threatened and habitual abortion, premature labor and other late accidents of pregnancy when administered early in adequate dosage. Similarly, in gynecologic practice the worth of this hormone has been amply demonstrated in the treatment of various ovarian deficiencies, such as dysfunctional uterine bleeding, oligomenorrhea, most

menometrorrhagias and in many cases of dysmenorrhea, senile vaginitis and endometriosis.

STUDY ON SIDE REACTIONS

Objection is sometimes made to the use of synthetic or natural estrogen because, in a certain percentage of cases, nausea or vomiting or both may occur among nonpregnant women. The incidence of side reactions following stilbestrol medication was given as 10 per cent by Novak¹ and 6.12 per cent by Hepp² in a discussion of a paper by Abarbanel and associates.³ Various in-

*Permission to do this work was granted by the Research Committee, Jefferson Davis Hospital.

1. Novak, E., J.A.M.A., 121:1129, 1943.
2. Hepp, J. A., J.A.M.A. 121:1129, 1943.
3. Abarbanel, A. R., Aranow, H., and Goodfriend, M. J., J.A.M.A., 121:1123, 1943.

investigators have shown that stilbestrol or the natural estrogenic hormones, when given on a comparable weight basis, produce an equal degree of nausea or vomiting.

USE OF STILBESTROL COMBINATIONS

For the past several years, I have been experimenting with various types of treatment for the purpose of overcoming the objection to nausea and vomiting in an otherwise valuable drug. In an earlier paper⁴ I stated, "We have found that the best and most efficient stilbestrol combination consists of micronized triple crystallized stilbestrol combined in one tablet with an ample dosage of B Complex vitamins including folic acid plus added Vitamin C. The administration of this form of stilbestrol therapy aided greatly in lessening stilbestrol reaction in forty consecutive nonpregnant patients. Thirty-eight experienced no vomiting; most patients had mild reactions. Forty nonpregnant patients who served as controls were given 6.25 milligrams of micronized stilbestrol without B Complex vitamins. Thirty-eight of the series experienced both nausea and vomiting." A later study of this problem with a larger series of patients has confirmed these findings.

Recently it has been established that folic acid and possibly other B Complex vitamins are essential in estrogen metabolism.⁵⁻⁸ The theory has been advanced that the B complex vitamins, especially folic acid, activate stilbestrol from an inactive, toxic drug to an active, nontoxic form of estrogen which no longer affects

the vomiting center of the brain, as does the inactive form of stilbestrol. As a consequence, nausea and vomiting do not occur or the incidence is greatly reduced.

For the past eleven or twelve years I have been using stilbestrol and more recently vitaminized, micronized stilbestrol (desPLEX) and micronized stilbestrol (des) for the treatment of endometriosis. It has been said that estrogens are contraindicated in endometriosis.⁹⁻¹¹ Goodall,¹² on the other hand, states: "It must be emphasized that endometriotic disease is an expression of endocrine imbalance." In a preliminary report¹³ he stated: "If endometriosis is due to an endocrine imbalance, what effects would estrogens have on endometrial implants?" Preliminary studies with vitaminized micronized stilbestrol or micronized stilbestrol for the treatment of endometriosis clearly demonstrated the value of these preparations for this condition. It was then decided to continue the investigation with a larger series of patients.¹⁴ The results of this study will be reported on 252 consecutive cases of endometriosis at a later date.

METHODOLOGY

The procedure and dosage schedule as outlined in table 1 have been in the main my method for treating endometriosis. The tablets are taken at 9 p.m. and the dosage increased as shown. The purpose is to keep the patient amenorrheic for from three to six months. The longer micronized stilbestrol is taken and

4. Karnaky, K. J., *Practical office gynecology*, Springfield, Illinois, Charles C. Thomas, 1947.

5. *Ibid.*

6. Hertz, R., *Effect of B vitamins on the endocrinological aspects of reproduction. Vitamins and Hormones*, 1946. 4:135, 1943.

7. Hertz, R., *Hormone Res.*, 2:161, 1948.

8. Jailer, J. W., *J. Clin. Endocrinol.* 9:557 1949.

9. Kline, I. J., and Dorfman, R. I., *J. Clin. Endocrinol.* 8:602, 1948.

10. Faulkner, R. I., and Riemenschneider, E. A.; *Am. J. Obst. and Gynec.* 50:560, 1945.

11. Meigs, J. W., *Ann. Surg.* 127:795, 1948.

12. Bushnell, L. F., *Am. J. Obst. and Gynec.* 55:915, 1948.

13. Goodall, J. R., *A study of endometriosis*, Philadelphia, J. B. Lippincott & Co., 1943.

14. Karnaky, K. J., *South M. J.* 41:1109, 1948.

TABLE 1
DOSAGE AND PROCEDURE SCHEDULE

0.05 mg. tablets	1.0 mg. tablets	25 mg. tablets
1 for 2 nights	½ for 2 nights	¼ for 3 nights
2 for 2 nights	1 for 2 nights	½ for 3 nights
3 for 2 nights	1½ for 2 nights	¾ for 3 nights
4 for 2 nights	2 for 2 nights	1 for 3 nights
5 for 2 nights	2½ for 2 nights	1¼ for 3 nights
6 for 2 nights	3 for 2 nights	1½ for 3 nights
7 for 2 nights	3½ for 2 nights	1¾ for 3 nights
8 for 2 nights	4 for 2 nights	2 for 3 nights
9 for 2 nights	4½ for 2 nights	2¼ for 3 nights
	5 for 2 nights	2½ for 3 nights
(then start 1.0	5½ for 2 nights	2¾ for 3 nights
mg. tablets)	6 for 2 nights	3 for 3 nights
	(then start	3¼ for 3 nights
	25 mg. tablets)	3½ for 3 nights
		3¾ for 3 nights
		4 thereafter

the larger the dose, the better are the results. The dosage may have to be increased even higher every four to six weeks because some patients will begin to bleed again after taking a certain dose constantly over a certain period of time. By increasing the dose, the patient is again made amenorrheic. Some patients will not stop spotting or bleeding even if larger doses are given. If this happens, then the uterine cavity is curetted gently for from 6 to 8 strokes with a Randall or Novak's curette in order to break loose the hyperplastic endometrium. The vagina is tightly packed with dry cotton for 24 hours. During this period, the endometrial tissue, in most cases, will be expelled onto the cotton in the vagina if ergotrate tablets are given (one every 3 hours for 8 to 10 doses).

If endometriosis is extensive and the patient has severe symptoms and does not wish to experience another such pain at the next men-

struation, the dosage of micronized stilbestrol is increased more rapidly to inhibit the next menstrual period. To prevent nausea from these larger doses, the patient is first given 5 cc. of B Complex concentrate intravenously and 5 cc. of B Complex intramuscularly (Bisbee). The patients take at home two special B complex vitamin tablets containing vitamin C plus tracer elements (Cevron) three times a day and at bedtime. The following method of administering des or desPLEX is used: 1.0 mg. is given every night at nine o'clock and every night increased 1.0 mg. until 6.0 mg. are being taken. Then ¼ of a 25 mg. stilbestrol tablet is increased every night until four 25 mg. tablets are being taken. If spotting or bleeding occurs during the treatment period, two 25 mg. tablets (50 mg.) are taken every 15 minutes until bleeding stops.

Pelvic examination is made every seven to ten days in order to de-

termine when the bound-down endometrial masses and pelvic organs have become freely movable. It usually requires from 3 to 6 months for the desired results. Some patients will require 200 to 400 mg. of micronized stilbestrol daily for 4 to 9 months in order to cause endometriosis to undergo atrophy and to keep the patients amenorrheic. If the patient wishes immediate relief during menstruation, then 200 mg. of des stilbestrol is given every 15 minutes until menstruation is stopped. B Complex concentrate vitamins are given intramuscularly and intravenously and 3 gr. of pentolin (2 capsules) are given by mouth and $\frac{1}{2}$ of a pentolin rectal suppository is inserted every hour until all nausea and/or vomiting is controlled.

DISCONTINUANCE OF DES OR DESPLEX

At the end of the treatment, when

the desired results are obtained, des-PLEX or des is gradually discontinued in the following manner: Each night for 2 nights, the patient takes 100 mg., 50 mg., 25 mg., $\frac{3}{4}$ of a 25 mg. tablet, $\frac{1}{2}$ of a 25 mg. tablet, $\frac{1}{4}$ of a 25 mg. tablet and stops. If flooding starts, $\frac{1}{4}$ of a 25 mg. tablet is taken every 15 minutes until the bleeding is checked. Bed rest also helps to check excess bleeding from estrogenic withdrawal. The giving of testosterone propionate (100 mg. intramuscularly) the day the patient starts to reduce the dose is of help.

CONCLUSION

A further preliminary report is given on the use of micronized and/or vitaminized, micronized stilbestrol for the treatment of endometriosis.

Sulphonamides in Cervical and Vaginal Infection

The clinical value of a "triple sulpha cream" was assessed in 110 patients with cervicitis, 3 with cervical polypus, 19 with cervical erosion, and 71 with vaginitis. The sulpha cream is a combination of sulpha-thiazole (3.42 per cent), N'-acetyl-sulphalinamide (2.86 per cent), N'-benzoylsulphanilamide (3.7 per cent), and urea peroxide (1 per cent), in a jelly base. Cauterization, coagulation or conization was applied to all patients with cervicitis, after which the sulphonamide cream was administered.

The patients were seen on alternate days for the first fortnight and then once a week until healing occurred. The vagina was cleansed at each visit and a cotton applicator saturated with mercurochrome was introduced into the cervical canal. The average time for complete heal-

ing was 5 to 6 weeks, as against 4 months for a group treated by the same method but without sulphonamides.

In the 71 patients with vaginitis the sulphonamide cream was applied daily; in 49 of these subjects the inflammatory changes and symptoms disappeared in approximately 3 to 4 weeks. Of the 38 patients with trichomonas infection in this group, 24 were "cured," 5 "improved," and 9 "unimproved." It is surmized that in the latter group the improvement probably was a result of the elimination of concomitant bacterial infectious agents rather than the destruction of the trichomonads. Local irritation from the use of the cream occurred in two of the patients.

(Jacoby, A. et al., *Am. J. Obst. & Gynec.* 63:1349, 1952.)

Radioisotopes and Medicine

Radioisotopes are finding increased use in general diagnosis and clinical practice.

REX L. HUFF, M.D., Berkeley, California

INTRODUCTION

The appearance of radioisotopes in medicine occurs in three principal categories, namely, diagnosis, therapy, and research. At present nearly all of the diagnostic and therapeutic applications are of definite value but are not unequivocal requisites of an excellent medical practice. On the other hand, the research applications are almost ubiquitous and of inestimable value and significance. It is propitious to make a comparison of the present status of isotopes in medicine to the state of advancement of bacteriology at the time when Koch and Pasteur first started using their microscopes. It has become evident that the practical applications of greatest value, coming as outgrowths of bacteriology, are first being made in our generation in the form of chemotherapy. It is not overly optimistic to expect that even more impressive medical progress will come about in less time as eventualities of the thoroughgoing

applications of isotopes in medical research.

The clinical use of radioisotopes is now demonstrated in all grades of elegance; from the powerfully effective teams of physician, physicist, mathematician, and chemist of the well-equipped laboratories of the large medical centers to the solo practitioner with his modest equipment. The present quantitative clinical radioanalysis is less complex and time-consuming than the usual technics of gravimetric, volumetric, and colorimetric analysis. The most time-consuming and unpleasant aspects of diagnostic, and especially therapeutic, applications is that of radiologic safety.

An active radioisotope program in a hospital or medical center will need expect that from 10 to 30 per cent of its budget will be for the express purpose of protection of personnel and patients. In this respect, isotopes are peculiar to anything heretofore seen and used in medicine. It is true that physicians con-

stantly prescribe and administer toxic substances which, when used in mistakenly large quantities, may be fatal. However, none of these substances traverse the walls of the container, as does the radiation from some isotopes, to attack the handlers or the patients. Roentgen ray machines and fluoroscopes are in general confined to a single location when they are generating radiation. Radioisotopes are constantly being transported by technical personnel and by patients. Each isotope has its individual physical and chemical qualities which govern its handling. The nearest analogy is a radium implant, but even this has been confined within the container and carefully removed once the treatment is over. This potential danger of radioisotopes has not prevented the vast industrial and military progress of the Manhattan Engineers and the Atomic Energy Commission, nor will it prevent the "much heralded" and "much looked for" benefits to medicine.

The physician has an excellent basic science background for understanding and using radiosotopes. Some physicians now making radioisotope applications have taken special short courses such as given by the Educational Division of the Oak Ridge National Laboratory where, upon graduation, the student is granted a scroll with the title "Dabber in Radioisotopes". Other physicians have spent much more time and effort in achieving background and technique.

Procurement permission for radioisotopes for medical use must be gained through the Atomic Energy Commission, unless the isotope is produced by equipment such as the cyclotron of a private university. Once permission for use is granted by the A. E. C. there are several sources of supply:

1. Oak Ridge National Laboratories.
2. Brookhaven National Laboratories.
3. Argonne National Laboratories.
4. Abbott Laboratories (through Oak Ridge).

By far the greatest quantity comes directly from Oak Ridge; however, many users are finding the chemical and bacteriological control, as well as the packaging offered by Abbott Laboratories, a useful service.

EQUIPMENT

Equipping a modest clinical radioisotope laboratory costs about \$2500. Such equipment would include (1) a scaler; (2) crystal and photomultiplier tube for liquid sample counting; (3) scintillation crystal and photomultiplier tube for *in vivo* counting; (4) support for items (3); (5) monitoring devices for radiological safety; (6) shielding for radiation; and (7) Gieger tube, support and shield for beta counting.

The \$2500 does not include the necessary equipment and expendable supplies which are usually present in a clinical laboratory, such as centrifuges and glassware.

This cost can be reduced from \$1000 to \$1500 with slight inconvenience if work is restricted to I^{131} , P^{32} , Fe^{59} , and Na^{24} .

THERAPEUTIC APPLICATIONS

Radiophosphorous: P^{32} —This was the first artificial radioisotope receiving therapeutic application. Shortly after Ernest Lawrence invented the cyclotron at Berkeley, his brother, John Lawrence, used P^{32} in the treatment of polycythemia vera, leukemia, and the lymphomas. Now, after more than fifteen years, there is general agreement that P^{32} constitutes the most important agent in the treatment of polycythemia vera, and that it is of definite usefulness in the handling of

the chronic leukemias. Much has been written on this subject by John Lawrence and others. Extensive application of P^{32} has been made by Low Beer in the treatment of localized skin cancer. This form of therapy is effective but is of doubtful advantage over the equally effective excision or X-radiation.

The localization of P^{32} in the form of colloidal chromic phosphate in the reticuloendothelial system following intravenous injection has been described by Dobson, Jones, and Goffman, but this property of localization has not been explored extensively therapeutically.

Radioiodine I^{131} — This isotope, of all, has received the most use in therapy. Its application has been chiefly in hyperthyroidism, metastasizing carcinoma of the thyroid, and in the production of myxedema in selected cases of intractable congestive heart failure or angina. In many respects, I^{131} offers an optimum form of therapy for hyperthyroidism, but there are some exceptions. Most physicians do not give the isotope in therapeutic amounts to women capable of bearing children because of the danger of excessive radiation producing genetic changes in the ova or of producing teratology. Although theoretically it would appear that the treatment of carcinoma of the thyroid was ideally suited for I^{131} , in practice there are only a few of such cases which respond favorably. Often the metastatic tissue has enough functional aplasia that it will not concentrate iodine.

Iodine 131 is ideally suited for the production of myxedema in cardiac cripples. However, the evaluation of such alteration in physiology in the presence of advanced disease is difficult. Blumgart is convinced that a significant number of patients falling into this category can be bene-

fited by I^{131} induced myxedema with maintenance of the BMR at 20-25 with small doses of thyroid extract.

Gold 198 — Considerable impetus has been given to the use of Colloidal Au 198 in the treatment of various forms of neoplastic disease because of the fact it spreads from the site of injection to adjacent lymphatic tissue harboring metastases. Apparently phagocytosis of the colloid occurs by the metastatic cells. Most of the work with colloidal radiogold is current and its precise status in the treatment of various forms of carcinoma remains to be determined.

DIAGNOSTIC USES

Radioiodine I^{131} — The diagnostic applications of this isotope are based in part upon its characteristic role in thyroid metabolism, but also upon other chemical and physical qualities.

For diagnosis of thyroid function a few microcuries are given per os or intravenously and one or more of the following procedures carried out:

1. 24 or 48 hour urinary excretion of I^{131} .
2. 24 hours uptake of I^{131} by the thyroid (determined by external scintillation counting over the thyroid).
3. A complete curve of I^{131} in thyroid for several days.
4. The ratio of plasma organic bound I^{131} to nonorganic bound I^{131} .

In general these procedures are more reliably carried out than a basal metabolism test. They do not measure the same thing as the basal metabolism test, but there is good correlation of many I^{131} thyroid diagnostic studies and other parameters of thyroid function.

Careful tracer (1-10 microcuries) studies of thyroid uptake are done

in some institutions preceding I^{131} therapy for the purpose of calculating the proper dose of radioiodine for therapy. The most elegant thyroid application of I^{131} in this relation is the automatic scanning of thyroid by a mechanically mounted gamma crystal counter resulting in a graphic representation of the geometrical configuration of I^{131} distribution in thyroid. This graphically depicted geometry has been used in a fairly reliable empirical formula for the calculation of thyroid size and weight, the latter being necessary in I^{131} dose calculations. I^{131} labelled thyroxine has been used for the determination of its turnover rate in the body. This type of diagnostic method, just being applied, may offer more in the way of delineating hypo and hyper metabolic disorders than other parameters in regular use.

Non-thyroid diagnostic applications of I^{131} have been based on the property of combination of serum albumin with I^{131} in vitro. Iodinated albumin offers an easy method for the determination of plasma volume. Also, it has been found that radio iodinated albumin shows a selective uptake by brain tumors. This has allowed for localization of the tumor by externally scanning the cranium with gamma counters. Iodine tagged diiodofluorescein has been similarly used.

Sodium 24—Since the delivery of ions from one part of the body to another depends primarily upon blood perfusion rates of the tissues, Na^{24} is used in the evaluation of peripheral vasculature efficiency. The patient, with a gamma counter over the extremity in question, is given an intravenous dose of the tracer;

the increase in counting rate with time is used as an index of vascular efficiency.

Iron 59—It has been found that the plasma turnover rate of iron is roughly proportional to the production rate of hemoglobin. An intravenous dose of radio iron may be given and the rate of disappearance determined. More elaborate studies by external gamma counting indicates the organ destination and ultimate function of the administered iron; for example bone marrow vs. liver, hemoglobin synthesis vs. iron storage.

Iron 59 attached to its normal protein carrier can be used for plasma volume determinations as is iodinated albumin.

Phosphorous 32—The chief diagnostic application of this isotope has been the determination of circulating red cell volume. This is done by incubating the patients' cells with a solution of $Na_2HP^{32}O_4$, injecting the tagged cells and determining the dilution. This method has the disadvantage of the necessity of maintaining sterility of the sample while preparing it.

RESEARCH USES

These applications are protean and ubiquitous. What we write today is history tomorrow. There are certain principles which guide and indicate the application of an isotope to a research problem which are worth indicating:

1. They are particularly useful in determining the rate of a reaction.
2. They offer a method for the determination of a quantity by the isotope dilution technique.
3. They can be used to identify metabolic intermediaries in a dynamic biochemical system.

The Treatment of Alcoholism

*The alcoholic may be helped
by use of drugs, psychotherapy,
and group treatment.*

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INTRODUCTION

The most democratic of illnesses, alcoholism is found as frequently in our most respected citizens as among those in the humbler walks of life. One finds in many instances that alcoholism is evidence of varying degrees of psychoneurotic personalities. Alcoholism in other patients may be representative of a minor psychosis, feeble-mindedness, psychopathic personalities, epileptic equivalents, or very occasionally, evidence of an escape from incurable physical disease. Alcoholism must not be overlooked as an evidence of psychosomatic conditions. Some patients may even show evidence of such illnesses as hypertension and/or duodenal ulcer in conjunction with alcoholism.

The question of some as yet unknown chemical metabolic ingredient as part of the underlying cause of alcoholism has not been discovered, but this may be a major factor in some few instances and a minor one in others.

After recognition that he is an alcoholic, it is essential for the patient to *desire treatment* on his own accord. As alcoholics in general have a tendency to reject with hostility suggestions, persuasion and being pushed into treatment by those close to them, a good friend who has an alcohol problem and who is under successful treatment is usually very helpful, provided tact is used rather than exhortation and nagging. This state is psychologically important and plays an important

part in the treatment through redirecting the patient's apparent stubborn and selfish drives to constructive and creative ends.

RECENT CHEMICAL AND ENDOCRINE APPROACHES

Disulfiram is a name given to the compound tetraethylthiuram disulfide, manufactured and sold under the trade name of Antabuse. This chemical compound is used by some medical therapists as an aid in attempting to get a beachhead for treatment on certain specially selected patients with alcohol problems. This compound was first noted during World War II as an agent which caused physical symptoms and complaints in workers in the rubber industry who later imbibed, or attempted to imbibe, alcoholic beverages.

The *Journal of the American Medical Association*, May 17, 1952, states:—

"The employment of disulfiram in the management of chronic alcoholism requires the consent and full knowledge of the patient coupled with the application of psychotherapeutic measures designed to rehabilitate the patient. It should be emphasized that disulfiram alone cannot be expected to remove the underlying maladjustment; hospitalization, psychiatric care, and attention to complicating disease are sometimes essential if the patient is to achieve emancipation from alcohol. Disulfiram serves primarily as a 'sobering crutch' on which the alcoholic may lean while a sincere effort is made to remove the underlying desire for alcoholic intoxication. In this respect, it is similar in function to the use of drugs such as amphetamine which depresses the appetite as an aid to the control of excessive food intake in obesity. Amphetamine and related cerebral

stimulant drugs are sometimes employed also as adjuncts in the rehabilitation of chronic alcoholics to overcome associated depressive and anxiety states. The pleasant effect of such stimulants is in contrast with the unpleasant reaction induced by means of disulfiram.

"Physicians who are unwilling or unable to institute other appropriate measures for the physical, emotional, and social rehabilitation of the alcoholic should not prescribe the drug. Likewise, patients who are unwilling, or for reasons beyond the effect of the drug, are unable to cooperate should not be placed on therapy with disulfiram. Without a sincere desire to stop drinking and to follow the treatment as prescribed by the physician, the drug alone provides little chance for a cure. In such circumstances it may do more harm than good. As with other aids in the management of chronic alcoholism, ultimate success depends on correction of the underlying maladjustment of the individual. It is concluded that disulfiram *may* become established as a useful adjunct in the management of selected and adequately supervised cases of chronic alcoholism."

In summary, disulfiram (Antabuse) at best is only an adjunct to the treatment of chronic alcoholism. Perhaps in certain cases it may enable a physician to obtain a beachhead for further successful therapy, but it is in itself not a cure for alcoholism. The patient must desire to want to take the chemical. When placing a patient on disulfiram the technic should be instituted in a hospital because of the severe physical reactions that can occur.

Adrenal Cortical Extract — The possibility that alcoholism is a metabolic disease has recently been discussed in literature. No one has de-

termed as yet whether alcoholism is primarily a metabolic disease or continued use of alcohol produces changes which result in an altered metabolism. Many workers in the field of medical research and also those with practical experience in the treatment of alcoholism feel that the endocrine treatment of alcoholism, both acute and chronic, with an adrenal cortical hormone is a good available therapeutic means for controlling symptoms resulting from primary or secondary endocrine disfunctions.

Lovell *et al* state: "Glandular therapy is not intended as a cure for drug addiction or for alcoholism nor as a mechanism to restore alcoholics to successful drinkers, but rather as a valuable aid in treatment of the sick, addicted personality."

McAllister states, "It (adrenal cortical extract) should be combined with the recognized treatment of the alcoholic, such as psychotherapy and rehabilitation."

The adrenal cortical hormone approach is a healthy one, and apparently is one method of aiding in eliminating the drying out period in acute alcoholism and lessening the recurrent craving for alcohol in certain people.

The present day treatment consists of psychotherapy, which helps the patient learn and understand the specific origin, nature, unsatisfied needs, and other contributing factors behind his psychoneurosis or lack of emotional maturity. At the same time, other physical adjuncts (if the patient is seen just after a bout), vitamins, controlled sedation, salt, sugar, food and insulin as and when indicated are used and the common-sense re-education is started, by using the re-education guides which are now used all over the world by physicians, hospitals, Alcoholics

Anonymous groups, religious groups, information centers and National and Local committees on the problem. They are obtainable by writing to the National Committee on Alcohol Hygiene, Inc., Baltimore 17, Maryland.

INDIVIDUAL TREATMENT

Treatment of the alcoholic patient depends, of course, on his condition. Delirium tremens or pre-delirium tremens in cases under 55, uncomplicated by bromides, pneumonia or obvious permanent organic brain changes, should be treated immediately—on the spot—by intravenous administration of 1,000 or 2,000 cc. of normal saline solution with 50 cc. of 50 per cent glucose per 1,000 cc., insulin, and heavy doses of vitamin B₁. Appropriate sedation is used to prevent convulsions resulting from the abrupt withdrawal of alcohol.

It should be remembered that treatment of alcoholics is not an exact science, nor does alcoholism have any specific. It just isn't possible to look into a text book and find a formula which will give automatic results.

Each patient must be taken as a wholly new and entirely different problem, the solution of which is unique.

Experience with non-deteriorated alcoholic patients indicates that successful results are accomplished by the following factors:

1. Careful selection of patients, not deteriorated, feeble-minded or psychotic.
2. Personality of the physician.
3. Vitamin and insulin therapy in controlled dosage with sedation as indicated to aid on the physical side.
4. Psychotherapy with emotional re-education.
5. Interpersonal relationship of patient and physician.

6. Suggestive influences.
7. Interviews with the mate and close relatives.
8. Full cooperation of the patient and his family and associates.
9. Continuous follow-up.

GROUP TREATMENT

Alcoholics Anonymous—This group organization consisting of individual members with alcohol problems has progressed with amazing rapidity. Many an alcoholic has been helped through Alcoholics Anonymous. Help is given and obtained through the use of religion and lay application of psychiatric principles.

Salvation Army—This organization, one of the finest human rehabilitating agencies in this and other countries, has had unheralded success in bringing back many men and women with alcohol problems. They have been very helpful in the "Skid Row" type of alcoholic. A further progressive step by this group is the opening of their new \$500,000 "drying-out" center on Third Street in New York City.

SUMMARY

1. The alcoholic of today is a sick person.
2. The alcoholic must want help and cannot be treated against his will.

3. He is not hopeless and 40 per cent to 50 per cent are "cured"—permanent abstinence from alcohol with some satisfaction in most spheres of life.
4. An alcoholic can never learn to drink like a so-called social drinker; therefore "Once an alcoholic always an alcoholic" (as far as alcohol is concerned).
5. Hospitalization is no longer usually necessary for the treatment of the alcoholic of today.
6. Adrenal cortical extract is now used as an aid in treatment of the sick, addicted personality.
7. Disulfiram (Antabuse) may become established as an adjunct in obtaining a beachhead in some patients, but only under very careful medical supervision.

To aid in the prevention of alcoholism, greater stress should be laid on sound physical and mental health habits and on the emotionally important elements of family and religious life, especially in the very early years of life. These, with other factors, will aid in giving a strong, healthy emotional makeup which will be better able to withstand the terrific sociological pressures of today and the future.

AMEBIASIS

Amebiasis, which was thought to be relatively rare in the first years of life, was discovered in 80 infants under one year of age among 872 cases of diarrhea in infants and children, an incidence rate of 9.2 per cent.

Orthostatic Hypotension

*Etiology, diagnosis,
and treatment of an often
overlooked condition.*

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Orthostatic hypotension is characterized chiefly by a sudden decrease in the normal blood pressure when the patient assumes the upright position. When the systolic blood pressure reaches 80 mm. of mercury or lower, marked weakness and syncope result. The characteristic signs and symptoms are faintness, weakness, dimness of vision, severe headache, cardiac arrhythmia, and syncope. The reaction to the upright position is usually most severe in the morning when the patient gets out of bed. Tachycardia and arrhythmia may be present in cases of orthostatic hypotension.

CAUSE

The essential physiologic factor is the failure of the return of an adequate amount of venous blood to the heart. This defect of inadequate venous return becomes evident in a very short time after the patient stands. Conversely, adequate circulation with a normal heart rate and

blood pressure follows resumption of a supine position. The cause of this disorder appears to be generalized abnormally low venous capillary tone.

The hemodynamics of the syndrome are shown by changes that take place in the retinal vessels with shift of posture. When the patient is supine, elevation of the legs produces retinal hyperemia, distention and tortuosity of the vessels (especially the veins), slight increase in blood pressure, somewhat slower pulse rate, and a shorter circulation time. When the legs are lowered, the retinal vessels shrink and the retina becomes less hyperemic. The upright position brings the circulatory defect into full play, causing in most patients extreme pallor of the disc and fundus, contraction of the vessels, marked drop in systolic blood pressure, accelerated pulse rate, rise of venous pressure, and a prolonged circulation time. These

changes are reversed when the patient lies on his back.

Pooling of abnormal quantities of blood occurs caudad as the patient assumes the erect position. This syndrome is eliminated when the pool of blood is shifted cephalad either with or without elevation of the lower extremities with the patient in the supine position. However, the syndrome is eliminated sooner when the legs are elevated. Because of this pooling of blood, when the patient is erect, failure of normal venous return occurs, producing anoxia with its signs and symptoms.

The electrocardiogram may show an abnormal rhythm with a depressed S-T segment on change in posture from the supine to the erect position. Normal sinus rhythm can be replaced by auricular and ventricular premature contractions and auricular fibrillation. Sinus rhythm can be restored by lying down and raising the legs. Myocardial anoxia seems to be responsible for these transient changes.

TREATMENT

Paredrine hydrobromide¹ given orally as a single dose, 100-200 mg. about 30 minutes before arising in

the morning is effective in many cases. This drug, by its vasopressor action, increases the capillary venous tone and venous return of blood to the heart. Occasionally a midafternoon dose of from 40 to 60 mg. of paredrine is very helpful. Norepinephrin is effective but too fleeting in its action.

Methoxamine² (vasoxyl of Wyamine) doses of 5 mg. given subcutaneously before arising in the morning has been found to be most effective. Its action becomes effective in from 1 to 2 minutes after injection and lasts for 15-30 minutes. Methoxamine is given with paredrine, as it acts more quickly than paredrine.

SUMMARY

Orthostatic hypotension should be suspected if extreme exhaustion is felt in the morning but decreases during the day, or if faintness, dimness of vision, headache, cardiac arrhythmia or unexplained syncope is produced by standing and is abolished by lying down.

1. Yuskis, A. S., and Griffith, G. C. *California Med.* 69:244, 1948.
2. Nathanson, M. H., and Miller, H., *Am. J. M. Sc.* 223:270, 1952.

NIGHT-BLINDNESS

Vitamin A (in animal liver) has been known as a remedy for night-blindness for 3,446 years as indicated in the Ebers papyrus. 1000 years later Hippocrates recommended for night-blindness: "The patient should eat once or twice an ox liver as big as possible, raw or dipped in honey."

Acute and Chronic Hypoventilation Syndromes

The author discusses the diagnosis and therapy of this frequently unrecognized clinical problem.

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Spontaneous hypoventilation is a common cause of much suffering and illness. Physicians rarely watch the pattern of a patient's breathing closely enough to recognize hypoventilation when it is present. Yet, the correct diagnosis is made by simple inspection — and proper treatment promptly yields excellent results.

PHYSIOLOGY

In humans, respiratory function is controlled by an elaborate system of physiologic devices, many of which function on the "feedback" principle^{1,2} and help maintain homeostasis. These signalling devices include the sensory nerve inflow from the chemoreceptors of the carotid gland, proprioceptors from the lungs and from striated respiratory and non-respiratory muscles, exteroceptors (including those of special sense), enteroceptors, and intrapsychic

channels. All of these neuronal signals converge on the respiratory nuclei of the medulla and pons. The neurons in the brain stem which control respiration through their outflow signals are said to have an intrinsic rhythm which can be modified by alterations in blood chemistry (changes in the pH, oxygen or carbon dioxide content), and by impinging neuronal signals from the sources enumerated above. The outflow channels from the respiratory neurones, in turn, control the amplitude and frequency of movements of the diaphragms, respiratory muscles, chest and abdomen, as well as the accessory muscles of respiration which are used only when the patient is making maximal respiratory effort.

If an emotionally stable person is asked to hold his breath until he is uncomfortable from increasing hypoxia and hypercapnia, then upon cessation of voluntary breath-hold-

1. Fulton, J. P.: *Textbook of Physiology*. Philadelphia, W. B. Saunders Co., 1949.
2. Tustin, A., *Scientific American* 187:48, 1952.

ing, the rate and amplitude of his breathing increase temporarily until the hypoxia and hypercapnia are corrected. Only then is normal breathing resumed.

However, when a patient is emotionally disturbed, prepotent intrapsychic influences can modify respiratory movements sufficiently to interfere with normal ventilatory functions. In psychogenically induced spontaneous hypoventilation, the respiratory act may be altered so that the respiratory rate is slowed, or the range of movement of thoracic, abdominal and diaphragmatic muscles is decreased, or both. These alterations tend to decrease respiratory minute volume markedly, often producing sufficient hypercapnia and hypoxia to create clinically significant symptoms and signs.

CHRONIC HYPOVENTILATION

The syndrome of chronic hypoventilation is the most common. Here, the patient often breathes at a normal rate—but the amplitude of both inspiration and expiration are diminished to the same extent. Or, there may be frequent periods of prolonged breath-holding for as long as 40 seconds, followed by regular or irregular shallow breathing. Such patients are unaware of their hypoventilation. They complain of fatigue, tension, anxiety, pressure in the chest, and occasionally of palpitation. A few have mild cyanosis. Some have a bradycardia suggesting increased vagal tone; but most have tachycardia.

ACUTE HYPOVENTILATION

The syndrome of acute hypoventilation results when expiration is inhibited more than inspiration, so that periodically the patient's lungs are so full of air that no amount of inspiratory effort can introduce fresh air into the lungs. The patient strug-

gles to inhale, having no awareness that he has "forgotten" to exhale. When exhausted from this struggle, he temporarily relaxes his inspiratory muscles and blows off some of the stale air. Then he can once more inhale some fresh air.

These cycles are repeated over and over again. Such a patient has acute anxiety, periodic cyanosis, fear of impending death from asphyxia, severe pain in the anterior portion of his chest (often he complains of precordial tightness and retrosternal oppression), is broken out in a sweat, has dilated pupils, and tachycardia, often with many ectopic beats.

DIAGNOSIS

The diagnosis of spontaneous hypoventilation rarely can be made by laboratory means either in the acute or chronic forms. Most patients having this syndrome modify their breathing as soon as they are connected to a pneumograph or spiograph. Thus, a graphic recording may show no evidence of hypoventilation even when direct inspection of the patient before and after the attempt to record respiration does show characteristic hypoventilation. Therefore, the diagnosis of spontaneous hypoventilation can be made only by careful inspection of the patient's breathing when he does not suspect that his breathing is being observed.³⁻⁵

Once the diagnosis of acute or chronic hypoventilation syndrome is made, the physician has the job of explaining and demonstrating to his patient the cause of the troublesome symptoms. The physician must teach his patient to breathe properly. This is done by having the patient prac-

3. Kaufman, W.: *The Common Form of Joint Dysfunction*. Brattleboro, Vermont., E. L. Hildreth and Co., 1949.
4. Kaufman, W., *Miss. Valley Med. J.* 73:138, 1951.
5. Wolf, S., *J. Clin. Invest.* 25:1201, 1947.

dice exhaling many times during each day, then inhaling 500 cc. of air—and breathing 16 such breaths per minute. When the patient is able to do this consistently, he loses all of the symptoms and signs caused by acute or chronic hypoventilation. To complete the treatment, the doctor should exteriorize and correct whatever emotional disorder initiated the syndrome of hypoventilation.

However, especially in the older age groups, the physician must be certain that he is not dealing with two separate problems: hypoventilation and early myocardial ischemia and infarction. Clinically, spontaneous hypoventilation indirectly may precipitate life-threatening myocardial hypoxia in those who already have narrowed coronary arteries.

The physician must also know that often spontaneous hypoventilation triggers off an attack of *hyperventilation*. The proper control of breathing, with an explanation of the cause of the patient's alarming symptoms, will relieve both types of respiratory dysfunction.

My clinical observations indicate that many chain smokers have spontaneous hypoventilation when they are not smoking. The only time that they have a relatively normal ventilatory exchange is when they are actually smoking. When such patients are retrained to breathe properly, they can often give up chain smoking without discomfort. In fact, some no longer have the need to smoke.

PSYCHOTHERAPY

The psychotherapy of hypoventilation is a highly individualized procedure. Some persons lose their tension and anxiety when they understand the physiologic basis of their symptoms, and have no other psychotherapy. With others, it is necessary to show how the hypoventila-

tion syndrome developed as a consequence of excessive grief, or as a consequence of having the death-wish and having it fulfilled through natural causes. Many persons develop this trouble from the fear of hearing criticism of their work, from listening to warning sounds of impending trouble—such as possible burglars—from being up during the night listening for the baby to cry and make its wants known, or from concentrating all one's attention on doing a delicate piece of work.

Some people hold their breath or reduce the amplitude and rate of breathing when they exert themselves physically. This occurs in stair-climbing, walking up hills, scrubbing and waxing floors, painting walls, and so forth. This habit pattern is of possible danger to individuals whose coronary arteries are narrowed by disease, since it may precipitate life-threatening myocardial infarction.

Usually, the patient develops confidence in his doctor as soon as the doctor proves the physiologic basis for the patient's troublesome symptoms and teaches the patient how to gain freedom from the hypoventilation syndrome. This makes it easier for the doctor to help his patient to get rid of undesirable emotional patterns of reacting which originally set off his hypoventilation syndrome.

SUMMARY

The psychogenically induced spontaneous hypoventilation syndrome is a common but frequently unrecognized clinical problem. The respiratory minute volume is decreased markedly because either the rate or amplitude of breathing, or both, are sub-optimal. When this continues for a sufficient period of time, enough hypoxia and hypercapnia are produced to create clinically significant symptoms and signs. The diagnosis

is made by inspection, since the mere suggestion that respiration is being measured or recorded instrumentally is capable of temporarily altering the pattern of the patient's respiration.

In the chronic forms, both amplitude and rate of breathing may be decreased, or the rate may be normal and both the amplitude of expiration and inspiration are equally decreased. There may be periods of prolonged breath-holding for as long as 40 seconds.

These patients are unaware of hypoventilating but usually complain of fatigue, tension, anxiety, pressure in the chest; a few seem mildly cyanotic, a few have bradycardia, but most have tachycardia.

In the acute forms, expiration is inhibited more than inspiration, resulting periodically in asphyxial crises. Patients with this syndrome have acute anxiety, cyclic cyanosis, fear of impending asphyxial death, anterior chest pain, precordial tightness or retrosternal oppression, dilated pupils, tachycardia, and often extrasystoles.

In both chronic and acute forms, exhalation of about 500 cc. of air followed by inhalation of about 500 cc. of air, repeated 16 times a minute, alleviates the condition.

The long-term therapy consists (a) in training the individual to breathe normally at all times and (b) in exteriorizing and correcting his emotional troubles which originally initiated his hypoventilation syndrome

Etiologic Factors in Cerebral Palsy

One infant in every 200 births shows the clinical signs of cerebral palsy, according to a survey made by the New York State Health Department. It occurs most frequently in premature children, in first-born and in corpulent infants born after prolonged labor. It is more prevalent among boys than girls. White children are more susceptible than colored, which may be due to the smaller average size of the new-born negro infant and the lower incidence of Rh negativity among the latter race.

Predisposing factors related to cerebral palsy may be of a hereditary or of a congenital nature.

Natal causes of cerebral palsy may be traceable to anoxia, asphyxia, analgesia (the respiratory center in infants is highly sensitive to morphine; obstetrical anesthesia, which causes maternal asphyxia, may like-

wise asphyxiate the fetus); birth-trauma; sudden transitional pressure changes, intra-uterine pressure being greater than the atmospheric, the abrupt change from one to the other may produce air emboli and ruptured blood vessels and hemorrhage; premature birth (the thinner and therefore weaker blood vessels of premature infants favor cerebral hemorrhage); and lack of vitamin K and resulting neonatal bleeding.

Postnatal occurrence of cerebral palsy may result from brain pathology after birth, such as trauma, infections, neoplasms, drugs, vascular disorders and anoxia. The number of patients afflicted with acquired cerebral palsy of the spastic and flaccid hemiplegia type attributable to cardiovascular accidents is said to now exceed one million.

(Deaver, G. G., *Bull. New York Acad. Med.* 28:532, 1952.)

Neisseria in the Genital Tract

The presence of non-gonococcal *Neisseria* in the genital tract constitutes a possible source of error in the bacteriologic diagnosis of gonorrhea. In an attempt at the full identification of *Neisseria* found in cultures from the genital tract of 1,575 patients, it was discovered that 3.4 per cent of *Neisseria* isolated from female patients attending a venereal diseases clinic were not gonococci; the corresponding figure for male patients was 1.5 per cent.

It is strongly recommended, therefore, that every laboratory which undertakes cultural examinations for gonococcus should be prepared to attempt its full identification by fomentation reactions, and should not be content with any less stringent criteria.

Wilkinson, A. E., *Brit. J. Venereal Dis.* 28:24, 1952.

Colonic Stasis

Classification of colonic stasis is based on x-ray observations of the emptying time of colonic segments; a roentgenographic evaluation of the common treatment methods revealed that a muciloid substance (Metamucil) was the least irritating and most effective drug in the most prevalent distal colon stasis. Enemata gave good results in rectal stasis only. Antispasmodics and sedatives had no efficacy at all. Mineral oil had little effect. Use of habit forming cathartics may be avoided in most instances.

(Barowsky, H., *Rev. Gastroenterol.* 2:145, 1952.)

Thalamic Syndrome

Vascular lesions in the thalamus frequently are characterized by excruciating pain at the side of the lesion, caused by light pressure or passive movements, or even developing spontaneously. The author has administered, in such cases, Benadryl, 400 to 600 mg. daily by mouth for up to two weeks or longer. Of 17 cases thus treated the results were very good in 5, satisfactory in 10, and doubtful in 2.

(Barris, R. W., *Neurology* 2:59, 1952.)

Chemical Sympathetic Block in Essential Hypertension

"An adrenergic blockade was established and maintained by oral medication with a new sympathetic blocking agent, 688-A (N-phenoxyisopropyl-N-benzyl-beta-chloroethylamine hydrochloride), in 11 patients with essential hypertension." Blockade was continuous when gelatin capsules were used. Dosage varied from 1 to 4 mg. per kilogram of body weight per day and was less with gelatin capsules. "A significant fall in recumbent diastolic pressure was obtained in 5 of the 11 patients. Significant lowering of the diastolic blood pressure in the upright position occurred in 9 of the 11 patients." Severe toxic reactions were not observed, but weakness, drowsiness, nasal stuffiness, and palpitations occurred.

(Moser M. et al. *Arch. Ind. Med.* 5:708, 1952.)

Clinical and Pathologic Aspects of Appendicitis

Of some 500 cases of acute surgical abdomen clinically diagnosed as acute appendicitis, during the period from November 1950 through July 1951, evidence of acute appendicitis as revealed by microscopic examination was found in 68.6 per cent. Normal appendices were present in 18 per cent. Three patients had parasitic infestations of the appendix, and one patient had carcinoid and mucocele in the appendix.

A positive correlation between leukocyte counts and microscopic diagnosis was observed in about 72 per cent of the cases. Over 75 per cent of the patients with confirmed acute appendicitis were operated on within the first 24 hours after the onset of symptoms. Variation of the appendix from the normal position was seen in 19 patients. About 80 per cent of these appendixes were acutely inflamed.

Positive correlation between gross descriptions and microscopic findings was found in about 91 per cent of the 500 appendixes examined. The average age of the patients on whom appendectomy was done approximated 22 years.

(Rubnitz, M. E., and Hansen, J. L., U.S. *Armed Forces M. J.* 3:1359, 1952.)

Parenteral Administration of Calcium

Authors state that Calphosan has been found to be effective in raising low serum calcium levels; after 4 weeks injection of 10 cc., the level remained, in most cases, normal for almost a year. Calphosan is a specially prepared, 1% solution of calcium lactate and calcium glycerophosphate in normal saline.

(Hoffmann, R. H., Abrahamson, E. M., Josephson, B. A., *Am. J. Digest. Dis.* 3:79, 1952.)

Sedimentation Rate in Acute Cholecystitis

The sedimentation rate offers a simple laboratory procedure which accurately indicates the course of the disease within the gallbladder. Day-to-day variations in this rate are more consistently correlated with changes in the severity of the disease than are any other laboratory or clinical findings, it is claimed. A rising or persistently elevated sedimentation rate is consistent with an increased severity of the local process within the gallbladder, and is a more accurate gauge of the disease in most patients than are clinical symptoms and abdominal findings. Leukocyte counts, temperature and pulse curves, and careful day-to-day observations of variations in abdominal manifestations are not accurate criteria by which the state or progress of the disease can be judged correctly.

In the group of nineteen patients treated by the author, the sedimentation rate was the only finding which was consistent with the pathologic process associated with the individual case of acute gallbladder disease.

(Hewlett, T. H., *U. S. Armed Forces Med. J.* 3:1267, 1952.)

Tuberculosis

The authors report on their experience with subcutaneous administration of large doses of dilute solutions of sodium PAS utilizing lyophilized hyaluronidase to expedite absorption. The authors recommend tentatively that for most situations requiring parenteral PAS, 12.5 to 18.75 Gm. of sodium PAS in a 1.5% solution be given subcutaneously over a three hour period, twice daily, with an interval of 8 hours.

(Fisher, B. M., Roberts, J., and Hinshaw, H. C. (*Am. Rev. Tuberc.* 64:557, 1951.)

Pain

Trigger areas may be blocked not only by physiologic saline solution but also by dry needling, if the trigger areas are thoroughly peppered with the needle. In clinical experience the order of efficiency would be procaine first, saline next and needling last. Results obtained by ethyl chloride spray in 40 cases of so-called "stiff neck", where pain and stiffness had been present for from 1 to 3 days, are presented. The spray was applied over the trigger areas of the neck muscles, the major one usually being in the trapezius. A large proportion of these patients showed complete and immediate relief of pain, and restoration of motion to normal during spraying. A certain proportion of them showed marked, immediate improvement but an hour or two later there was some recurrence of stiffness and pain; yet within a few hours the neck motion was normal. In another group of patients the range of motion improved at once by about 50%. The next day the range of motion was the same as after spraying. There were a few patients in whom the spray was apparently ineffective. Such cases can often be managed by direct infiltration of trigger areas with procaine.

(J. Travell, in *Transactions of the Second Conference on Connective Tissue*, Jesial Macy Jr., Foundation, New York, 1952).

Depression

In emotional depressions which are caused by physical conditions such as menopause, allergic reactions, or trauma to the head, dexamyl tablets are found to be helpful; they contain $\frac{1}{2}$ gr. of amobarbital and 5 mg. of dextro: amphetamine sulfate. One tablet is given t.i.d.

(Drayton, W., Jr., *Pennsylvania M. J.* 51:949, 1951.)

Toxemia in Pregnancy

The author has tried veratrum derivatives in the treatment of pregnancy toxemia. His method is as follows: continuous intravenous infusion of 5% glucose in water after admission of the patient to the hospital. A single injection of 1 cc. of Verenteral diluted in 10 cc. of 5% glucose in water was given through the infusion tubing over a two to three minute period. About an hour later, Verenteral was added to the intravenous infusion in the amount of 1 cc. per 100 cc. of 5% glucose solution. 5 cc. of 50% magnesium sulfate were given intramuscularly within the first hour and then every six hours. After 8 to 48 hours of intravenous therapy, intermittent intramuscular injection of 0.2 cc. of Veraflex was substituted, every 2 to 4 hours until delivery and was continued for 2 to 3 days post-partum. The authors' conclusion is that Verenteral and Veraflex are adequate preparations for the treatment of preeclampsia and eclampsia.

(Baird, W. W., and Assali, N. S., *Am. J. Obst. & Gynec.* 62:1093, 1951.)

Hemiplegia

The author advised infiltration of the stellate ganglion of the side opposite to the paralysis as soon as possible beginning with 10 cc. of 1% percarine, repeating 6 hours later with 20 cc. and then an infiltration each day for two weeks. It seems advisable to infiltrate the paralyzed side from time to time and even to associate with stellate ganglion block a lumbar infiltration. The author thinks that sympathectomy is indicated only in patients who have had several cerebral episodes. While the best results are obtained in the newest cases, a positive result may be obtained even after several years.

(Leriche, R., *Presse Med.* 6:153, 1952.)

THERAPEUTIC TRENDS

Local and Regional Analgesic Injections in Painful Musculoskeletal Conditions

Regional blocks by paravertebral route to infiltrate spinal or sympathetic nerves and ganglia cranial nerves and ganglia, or to anesthetize the nerve supply to a region or part. Local block is the infiltration of procaine at the site of palpable maximum tenderness, at a 'trigger point'. Intravenous procaine recently had been advocated for the treatment of arthritis and other neuro-musculoskeletal disorders. Ethyl chloride spray is used for surface anesthesia and analgesia by freezing peripheral, painful areas. In local analgesia the sore points are localized, a simple skin wheal is made for entry of the deep injection. A preliminary subcutaneous introduction of a few cc. of normal saline solution serves as control. No more than 5 cc. of ½% procaine solution is injected at first to establish the patient's tolerance. In peripheral tissues 2-20 cc. of a ½% or 1% solution may be employed subsequently. In acute traumatic lesions 3 to 5 daily injections sometimes are necessary. In chronic painful conditions 2 injections a week suffice until improvement occurs, then once every 5 to 7 days. Minor procaine reactions are encountered in 30% of cases: dizziness, pallor, tachycardia, palpitation, weakness, nausea, 'remoteness', occasionally fainting.

(Steinbrocker, *Arizona Med.* 3:27, 1952.)

Leg Ulcers and Varicose Veins

Present-day treatment of varicose veins consists in obliteration of the dilated parts by injection; most widely used substances are 66 per cent glucose and 10 to 25 per cent sodium chloride solutions. The latter ones are preferable. About 8 to 10 cc. of glucose and 2 to 4 cc. of sodium chloride solution are necessary for one injection. The site of injection is compressed for a short time, the leg is elevated and to the entire region of the varicose veins a compressive bandage is applied for a few days. The injections should be spaced in 10 to 14 days intervals. After injection the obliterated area may show an inflammatory reaction, which subsides after 2 to 3 weeks. If the varicosities are very extensive surgical treatment will be necessary, combined with injection therapy. Ulcers may be treated with ointments: 16 per cent naphthalan ointment in lanolin, with 4 per cent hog lard and 10 per cent zinc oxide, placed thickly on gauze and covered by cotton and a compressive bandage. Cod liver oil is also recommended. Treatment of varicose ulcer must be continued until a firm skin has formed; elastic stockings must be worn a long time. In rare cases surgery is indicated for the treatment of these leg ulcers: skin and fascia are divided and all cutaneous tension is eliminated. Healing of even stubborn ulcers will be aided by bed rest.

(Jaeger F., *Deutsche med. Wchnschr.* 77:422, 1952.)

Treatment of Carbuncles with Penicillin

Fourteen patients with carbuncles were treated with local penicillin injections and the results were compared with those previously obtained with parenteral penicillin, plus incision or excision under anesthesia.

The local injections of penicillin were made into the area peripheral to the inflammatory zone, not into it. Four portals for injection were employed, thus placing 300,000 to 600,000 units of penicillin about the lesion. The patient was then put to bed, and penicillin was injected intramuscularly intermittently to guard against "metastatic infection." No incising or excising was done, except that necrotic tissue, where present, was removed by local debridement.

All the lesions healed well, and there was no instance of metastatic infection. Usually relief of pain was experienced within 8 to 16 hours, and at the end of 24 to 48 hours the condition was either stationary or ready to resolve.

The average hospital stay for the latter series of patients was 4.9 days, as against 9.2 days for parenteral penicillin plus surgery, and 13.7 days for patients treated without penicillin.

Healing time was 12.6 days for the first, as against 42 and 31 days for the second and third series of patients, respectively.

These results seem to indicate that local injection therapy produces a more rapid healing of the lesion after a briefer period of hospitalization, without an increase in complications. However, it is also cautioned that further study will be necessary to determine if there are any specific contra-indications to this treatment.

(Dale, W. A., and Haug, C. A., *J.A.M.A.*, 149: 527, 1952.)

A New Curare Antagonist in Electroshock Therapy

A new curare antagonist, "Tensilon" (Hoffman-La-Roche), and a new technic for the administration of pentothal sodium (d-tubocurarine) are described.

Clinical observations and electromyographic studies revealed that the administration of a dose of 2.5 mg. of Tensilon usually counteracted effectively each 3 mg. dose of d-tubocurarine. The new drug was administered some 2000 times to curarized patients without occurrence of alarming side reactions. Doses as large as 20 mg. produced only minor reactions, such as excessive perspiration and mild salivation. Intravenous doses ranging from 10 to 20 mg. successfully counteracted serious curare depression attributable to surgical anesthesia. The ventilation rate of the patients thus treated with Tensilon showed a substantial increase within 90 seconds.

(Faulconer, A. Jr., Lambert, E. H. and Rome, H. P., *Neurology* 2:226, 1952.)

Treatment of Hypoprotebinemia

Eight patients with hypoprotebinemia resulting from dicumarol therapy and one patient in whom the same condition followed the self-administration of 8 to 10 aspirin tablets daily for about one month were evidently successfully treated with vitamin K. The oral therapy with this vitamin in initial doses of from 333 to 1000 mg. is stated to have produced excellent responses as measured by clinical improvement and rise in prothrombin activity (Quick method). This is believed to be the only report on the oral use of vitamin K in the treatment of hypoprotebinemia to be found thus far in the literature.

(Reid, R. A., *Quart. Bull. North. U. N. Sch.* 25:292, 1952.)

Myocardial Infarction

Authors previous work has shown that those lipoproteins migrating with rates between 10 and 20 Svedberg units—the Sf10-20 class of proteins — are associated with human atherosclerosis. Authors studied this class of lipoproteins in the blood of a large group of patients with coronary artery disease over a one to one and one-half year period. Recurrence of myocardial infarction in patients with previous infarcts, and occurrence of infarction in patients with angina pectoris, developed predominantly in that part of the group showing the highest Sf 10-20 concentrations over the period of observation. Low-fat, low-cholesterol dietary management of patients with coronary artery disease was effective in reducing average Sf 10-20 levels. This reduction was associated with a marked reduction in rate of new myocardial infarctions in the group. Clinically, administration of 20 to 100 mg. of heparin produced dramatic relief of angina pectoris in 30 of 32 patients for periods of 3 to 10 days following a single injection.

(Lyon, T. P. et al, *Arch. Int. Med.* 3:421, 1952.)

ACTH and Cortisone vs. Salicylates

A comparison of the biological effects of cortisone and ACTH with those of the salicylates revealed many similarities and rather few differences. The results of this comparison, as based on the study of the available literature, are tabulated and briefly summarized under 17 subject headings denoting as many different biological effects, both similar and dissimilar.

(Hallman, H. F., *J. Clin. Endocrinol.* 12:454, 1952.)

Granuloma Inguinale

On the basis of experiences with 295 cases the authors recommend antibiotics for the treatment of granuloma inguinale. Streptomycin may be administered in divided doses of 4 Gm. per day for a period of five to ten days. In a few instances resistance to the drug or toxic reactions were encountered. Terramycin may be administered per mouth, 2 Gm. daily, for ten or twenty days or even longer. Side-effects such as headache and nausea are rare; the therapeutic effect in all treated cases (36) was satisfactory. Aureomycin also is given orally in doses of 500 mg. every six hours (daily 2 Gm.) for a period of ten to twenty days. There may be persistent lesions after termination of the treatment, but they disappear in the majority of the cases although repetition of the treatment may become necessary. Gastrointestinal reactions are slight. Chloromycetin is administered in the same way as aureomycin, yet the treatment period is much longer and in severe cases a treatment schedule of seventy days or more may be anticipated. The results are satisfactory. Side reactions such as nausea or dermatitis have been observed.

(Greenblatt, R. E., et al., *Am. J. Syph., Gonorr. & Ven. Dis.* 36:186, 1952.)

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Sugracillin 250 M: Flavored granules of buffered crystalline penicillin G potassium. When sufficient water is added to fill the bottle, Sugracillin provides 60 cc. containing 250,000 units of penicillin in each 5 cc. (teaspoonful).

Used in: Treatment of infections caused by pneumococci, staphylococci, streptococci, Vincent's organisms, and gonococci. Of particular use in pediatrics.

Dosage: Average dose for adults and children is an initial dose of two teaspoonfuls (500,000 units) followed by 1 to 2 teaspoonfuls every 4 hours.

The Upjohn Company,
Kalamazoo, Michigan

Chibeece: Liquid, containing in 5 cc. vitamin A, 3000 U.S.P. units; vitamin D, 1000 U.S.P. units; thiamine hydrochloride, 1.5 mg.; riboflavin, 1.2 mg.; vitamin B₁₂, 3 mcg.; nicotinamide, 10 mg.; and ascorbic acid, 60 mg.

Used in: Deficiency states.

Dosage: Adults, 2 to 4 teaspoonfuls daily; pediatric dose, 1 teaspoonful daily in 3 divided doses.

Chicago Pharmacal Company,
Chicago 40, Illinois

Bacimycin: Tablet containing neomycin, 25 mg., and bacitracin, 2,500 units.

Used in: Amebiases and infectious diarrhea.

Dosage: Adults, 1 to 3 tablets, 4 time daily; infants, 1 tablet every 6 hours; children, 1 or 2 tablets every 6 hours.

Walker Laboratories, Inc.,
Mount Vernon, New York

Furacin Soluble Powder: Contains 0.2 per cent of nitrofurazone N.N.R. dissolved in Carbowax.

Used in: Surface bacterial infections.

Dosage: As indicated.

Eaton Laboratories, Inc.,
Norwich, New York

Erythrocin: Tablet containing 0.1 Gm. of erythromycin.

Used in: Treatment of pharyngitis, tonsillitis, scarlet fever, erysipelas, pneumococcal pneumonia, osteomyelitis, pyoderma.

Dosage: Total daily dose is 0.8 to 2 Gm., depending on severity. Pediatric dose not yet determined.

Abbott Laboratories
North Chicago, Illinois

Nydrazid Injection: Injectable form of isoniazid.

Used in: Antituberculosis agent for patients who cannot take oral preparations.

Dosage: As indicated.

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Neo-Synephrine Ophthalmic Viscous: Solution of 10 per cent of neosynephrine hydrochloride with methylcellulose.

Used in: Vasoconstrictor and mydriatic.

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